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Better Diet Quality before Pregnancy Is Associated with Reduced Risk of Gastroschisis in Hispanic Women[1–3]

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Abstract

Background: Gastroschisis is unique because of its substantial risk in pregnancies of adolescent women. Adolescents may have poor diet quality, which places them at higher risk of gastroschisis.

Objective: We investigated whether better maternal diet quality, measured by 2 different indices, reduced the risk of gastroschisis.

Methods: We used case-control data from the National Birth Defects Prevention Study to investigate maternal diet quality among 1125 gastroschisis cases and 9483 controls (estimated delivery dates between 1997 and 2009). Cases were ascertained from 10 U.S. birth defect surveillance systems. Control subjects were randomly selected from birth certificates or hospital records. Using a 58-item food-frequency questionnaire, interviewers queried mothers about their average food and cereal intake during the year before conception. Diet quality scores [Diet Quality Index (DQI) and Mediterranean diet score (MDS)] were calculated using specific components. Women were excluded if they consumed <500 or >5000 kcal/d, reported pregestational diabetes, or had >1 missing food item. Quartile-specific adjusted ORs (aORs) were calculated, using as reference the lowest quartile.

Results: Overall, we observed a statistically significant decrease with increasing diet quality for both the DQI and MDS. When stratified by maternal race/ethnicity, this finding was confined to Hispanic women. Among Hispanic women, the risk of gastroschisis decreased significantly with increasing DQI quartiles: quartile 2, aOR = 0.58 (95% CI: 0.40, 0.86); quartile 3, aOR = 0.52 (95% CI: 0.36, 0.79); and quartile 4, aOR = 0.48 (95% CI: 0.32, 0.76). Increasing diet quality, as measured by the MDS, showed reduced risk of gastroschisis among women, mostly Hispanic, who were born outside the United States: quartile 2, aOR = 0.62 (95% CI: 0.33, 1.16); quartile 3, aOR = 0.51 (95% CI: 0.28, 0.94); and quartile 4, aOR = 0.50 (95% CI: 0.28, 0.90).

Conclusions: Increasing diet quality was associated with a reduced risk of gastroschisis only among Hispanic and foreign-born women, but these findings require replication. J. Nutr. 144: 1781–1786, 2014.

Introduction

Gastroschisis is a paraumbilic abdominal wall defect where a prolapsed midgut, and sometimes other organs, without a membranous covering, float freely within the amniotic fluid (1). In the United States, gastroschisis prevalence increased from 2.32 to 4.42 per 10,000 births between 1995 and 2002 and was 7 times higher among women <20 y of age than women aged 25–29 y (1). The basis of the strong and consistent association between young maternal age and gastroschisis is still unclear. To try to understand the biologic underpinning of this association, investigators have focused on factors that are more common in younger women, including suboptimal nutrition. For example, current recommendations based on the 2010 U.S. Dietary Guidelines emphasize the consumption of fruits, vegetables, legumes, whole grains, nuts, and seeds (2). Despite these recommendations, women of reproductive age—and adolescents in particular—are less likely to consume the recommended daily intake of fruits and vegetables, whole grains, and dairy (3–7). Maternal nutrition before and during pregnancy is an important determinant for

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[3] Supplemental Table 1 is available from the "Online Supporting Material" link in the online posting of the article and from the same link in the online table of contents at http://jn.nutrition.org.
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reproductive health and embryo/fetal development (8,9). Poor nutrition, assessed by single nutrients, is known to play a role in adverse outcomes of pregnancy (10) and has recently been implicated as a risk factor for several types of birth defects (11–16).

We previously investigated single micro- and macronutrients and their association with gastroschisis and did not observe evidence of worse intake among case mothers (17). Previous studies also do not demonstrate consistent findings or patterns of nutrient deficiencies. Thus far, increased risk of gastroschisis was reported in single studies with low levels of α-carotene and glutathione (18), and zinc (19), and with high levels of total and saturated fat (20), linoleic acid (21), and nitrosamines (18). Cánovas-Conesa et al. (22), based on a 98-item FFQ, reported that a diet in early pregnancy (11 case women; 34 control women) rich in oleic acid and vegetable products reduced the risk of gastroschisis. Although investigating single nutrients may provide clues, this method does not provide a comprehensive assessment of prepregnancy nutritional status because food choices are not based on single nutrients (23). Diet quality indices are more likely to reflect overall dietary patterns than single nutrients or food groups (24). Using diet quality to assess maternal nutritional status has been recently applied to investigate its association with birth defects. A statistically significant reduction in risk with increasing diet quality was observed for neural tube defects and oral facial clefts (23) but not for hypospadias (25) or microtia/anotia (16). With respect to gastroschisis, Paranjothy et al. (26) reported a reduced risk of gastroschisis among women consuming more fruit and vegetables during the first trimester. The purpose of the current study was to further investigate whether diet quality was associated with gastroschisis by using data from the National Birth Defects Prevention Study (NBDPS).[6] We chose 2 validated diet quality indices revised by Carmichael et al. (23) to incorporate pregnancy-related diet and alcohol recommendations: the Diet Quality Index (DQI) and the Mediterranean diet score (MDS). Although there are many useful diet quality indices available in the literature, the DQI reflects U.S. dietary recommendations, includes a combination of foods and nutrients, and has been adapted to pregnancy. The Mediterranean diet represents a food group–based score that was assessed in relation to many chronic diseases but rarely in the context of reproductive health; as such, the MDS provides a potentially interesting contrast to the DQI.

Subjects and Methods

The NBDPS enrolled eligible case and control mothers from 10 sites (Arkansas, California, Georgia, Iowa, Massachusetts, New Jersey, New York, North Carolina, Texas, and Utah) to investigate environmental and genetic risk factors for birth defects with unknown etiologies. This large U.S. population–based study included cases (i.e., live births, stillbirths, and pregnancy terminations) identified from these 10 surveillance systems with use of strict eligibility criteria (27,28). Randomly selected, healthy, live-born infants identified from either the state birth certificate files (AR: 2000–2003; GA: 2001–2003; IA, MA, NC, NJ, UT) or birth hospitals (AR: through 1999; CA, GA: through 2000; NY, TX) served as controls and represented the population from which the cases arose (28). Cases with known chromosomal or single-gene disorders were not eligible. Trained interviewers administered a computerized-assisted telephone interview (CATI) to case and control mothers 6 wk to 24 mo after their estimated date of delivery (28). One clinical geneticist was responsible for clinically reviewing each birth defect case group to assess their eligibility status and determine whether the case was isolated or multiple. Multiple defects comprised ≥2 unrelated major malformations occurring in 1 infant, e.g., an infant with gastroschisis and a congenital heart defect would be considered a multiple defect. Verbal consent was obtained before the telephone interview, and all sites maintained their own annual institutional review board approval.

Study subjects

For this analysis, we excluded all gastroschisis cases with a phenotype suggestive of limb-body wall complex or amniotic band sequence. We identified 1207 eligible gastroschisis cases and 10,200 controls with maternal interview data based on estimated dates of delivery from October 1, 1997 through December 31, 2009 (NBDPS analytical tools, v9).

Dietary quality assessment

The validated Willett (29) 58-item FFQ was administered as part of the CATI that included a commonly used serving size for each item (30). Interviewers were trained to read each food item and query the participant to determine their average frequency of consumption based on the food item's specific serving size during the year before their pregnancy. Participants were instructed to state "never or none" for those foods that were consumed <1/mo. Participants were also queried on the type and amount of cereal consumed and sodas or soft drinks using additional questions separate from the FFQ. The reported average intake of food items and cereal was used to estimate the mean daily intake for specific foods {[sum (servings/d × gm/serving for each food item in the component group)] / [mean gm/serving of all foods in the component group]} [see Supplemental Tables 1–3 from Carmichael et al. (23)]. For sweets, the number of servings/d of soda or soft drinks was added to the mean servings/d of sweets from foods listed in the group. Data for these nutrient calculations were derived from the SR19 version of the USDA's National Nutrient Database for Standard Reference (31).

We followed the diet quality scoring approach as described by Carmichael et al. (23). However, instead of ranking first by quartiles, we deviated slightly by using food group–specific deciles (scored 0–9) to reduce the ties at the cut-off points to create the overall scores for the diet quality indices. Diet quality scores (DQI and MDS) were calculated based on data derived from the FFQ that included specific components, with some overlap, for the 2 indices (**Table 1**).

DQI. This score reflects the recommendations made by Bodnar and Siega-Riz (32), which incorporate dietary components important during pregnancy. For this study, the DQI was modified to fit the NBDPS semiquantitative FFQ (23) from the more quantitative approach of the

TABLE 1 DQI and MDS components[1]

Component	Scoring	DQI	MDS
Fat (%)	–	●	—
Folate	+	●	—
Iron	+	●	—
Calcium	+	●	—
Fruits	+	●	●
Grains	+	●	●
Sweets	–	●	●
Vegetables	+	●	●
Fat ratio[2]	+	—	●
Fish	+	—	●
Legumes	+	—	●
Meat	–	—	●
Dairy	–	—	●

[1] – indicates a negatively scored component; + indicates a positively scored component; — indicates that the component was not included in score; and ● indicates that the component was included in score. DQI, Diet Quality Index; MDS, Mediterranean diet score.
[2] Ratio of monounsaturated to saturated FA intake.

[6] Abbreviations used: aOR, adjusted OR; CATI, computerized-assisted telephone interview; DQI, Diet Quality Index; MDS, Mediterranean diet score; NBDPS, National Birth Defects Prevention Study.

DQI during pregnancy (31). The DQI was based on the recommendations from the 2000 dietary guidelines and the 1992 food guide pyramid. The beneficial components (folate, iron, calcium, fruits, grains, and vegetables) were scored 0–9 (lowest to highest), and the negatively scored components (percentage of total fat, sweets) were scored 9–0 (highest to lowest).

MDS. The typical Mediterranean diet serves as the basis for this measure developed by Trichopoulou et al. (33,34) and revised by Hu et al. (35) to include fish. The beneficial components [vegetables, legumes, fruits, grains, fish, and fat ratio (high monounsaturated FAs to saturated FAs)] were scored 0–9 (lowest to highest), and the negatively scored components (meat, dairy, and sweets) were scored 9–0 (highest to lowest). The Mediterranean diet included alcohol as a beneficial component. However, because alcohol is not recommended during pregnancy, we excluded this from the beneficial component scoring as recommended by Trichopoulou et al. (34).

Total scores for the diet quality indices were summed for controls (DQI range: 0–72; MDS range: 0–81), and these distributions were used to determine the cut-off points for the diet quality–specific quartiles for all analyses.

Exclusions and statistical analysis

We excluded women who met the following criteria: *1*) reported a mean daily energy intake <500 and >5000 kcal (45 cases; 332 controls); *2*) had ≥2 food items on the FFQ that were missing or unknown (27 cases; 145 controls); and *3*) reported pregestational diabetes (10 cases; 240 controls). After these exclusions, 1125 cases and 9483 controls were available for analysis.

Crude ORs with 95% CIs were estimated with unconditional logistic regression for descriptive characteristics. Multivariable logistic regression was used to calculate adjusted ORs (aORs) with 95% CIs based on the a priori inclusion of the following covariates: maternal age (<20, 20–24, 25–29, ≥30), race/ethnicity (non-Hispanic white, Hispanic, other), prepregnancy BMI (<18.5, 18.5–24.9, 25.0–29.9, ≥30.0 kg/m^2), first trimester cigarette smoking (yes, no), and energy intake (kcal). aORs (95% CI) are presented by quartiles and for both the DQI and MDS; the lowest quartile served as the reference group for all analyses. We conducted post hoc analyses for both the DQI and MDS. We stratified by maternal race/ethnicity and used the Cochran-Armitage trend test to evaluate the overall and race/ethnicity–specific aORs of the DQI and MDS. Stratified analyses were also conducted for maternal age, birthplace, smoking, periconceptional folic acid–containing supplements, prepregnancy BMI, and maternal education (a crude measure of socioeconomic status). All analyses were conducted by using SAS 9.3 (SAS Institute).

Results

Compared with control mothers, case mothers were more likely to be younger, of Hispanic ethnicity, have a lower prepregnancy BMI, be less educated, smoke cigarettes, not consume folic acid–containing supplements, and be primagravida (**Table 2**). Among cases and controls, mean diet quality scores were lowest for women <20 y of age than the other age groups, but these differences were small (**Supplemental Table 1**).

Overall, there was a statistically significant downward trend in the risk of gastroschisis with increasing diet quality for both the DQI and MDS (**Table 3**). Stratified analysis for maternal age, birthplace, smoking, periconceptional folic acid–containing supplements, prepregnancy BMI, and maternal education did not change the overall findings for the DQI. Stratification by self-reported maternal race/ethnicity revealed statistically significant reduced risks with increasing DQI and MDS quartiles, among both Hispanic women and other race/ethnicities (Table 3). Specific individual DQI components (i.e., folate, iron, calcium, fruits, grains, vegetables, fat percentage, or sweets) did not explain these findings among Hispanics (data not shown). Numbers in the diet quality quartiles were too small to stratify further among the

TABLE 2 Characteristics among case and control mothers, NBDPS, 1997–2009[1]

Characteristics	Cases (*n* = 1125)	Controls (*n* = 9483)	Crude OR (95% CI)
Age, y			
<20	419 (37.2)	946 (10.0)	6.77 (5.58, 8.20)
20–24	460 (40.9)	2163 (22.8)	3.25 (2.70, 3.91)
25–29	173 (15.4)	2643 (27.9)	1.0
30–34	59 (5.2)	2425 (25.6)	0.37 (0.28, 0.50)
≥35	14 (1.2)	1306 (13.8)	0.16 (0.10, 0.28)
Race/ethnicity			
White, non-Hispanic	579 (51.5)	5603 (59.1)	1.0
Hispanic	349 (31.0)	2186 (23.1)	1.55 (1.34, 1.78)
Other	197 (17.5)	1688 (17.8)	1.13 (0.95, 1.34)
Missing	0 (0)	6 (0.1)	—
Education, y			
<12	313 (27.8)	1570 (16.6)	1.0
12	439 (39.0)	2252 (23.7)	0.98 (0.83, 1.15)
>12	360 (32.0)	5611 (59.2)	0.32 (0.27, 0.38)
Missing	13 (1.2)	50 (0.5)	—
Preconception BMI			
<18.5	99 (8.8)	498 (5.3)	1.31 (1.04, 1.65)
18.5–24.9	749 (66.6)	4944 (52.1)	1.0
25.0–29.9	190 (16.9)	2088 (22.0)	0.60 (0.51, 0.71)
≥30.0	55 (4.9)	1561 (16.5)	0.23 (0.18, 0.31)
Missing	32 (2.8)	392 (4.1)	—
Cigarette smoking[2]			
No	708 (62.9)	7755 (81.8)	1.0
Yes	412 (36.6)	1714 (18.1)	2.63 (2.31, 3.01)
Missing	5 (0.4)	14 (0.1)	—
Periconceptional folic acid[3]			
No	186 (16.5)	1136 (12.0)	1.0
Yes	925 (82.2)	8269 (87.2)	0.68 (0.58, 0.81)
Missing	14 (1.2)	78 (0.8)	—
Gravidity			
0	554 (49.2)	2825 (29.8)	1.0
1	315 (28.0)	2752 (29.0)	0.58 (0.50, 0.68)
2	124 (11.0)	1878 (19.8)	0.34 (0.28, 0.41)
≥3	132 (11.7)	2028 (21.4)	0.33 (0.27, 0.41)
DQI[4]	34.1 ± 13.9	36.0 ± 13.6	—
MDS[4]	37.2 ± 9.9	39.4 ± 9.9	—

[1] Values are *n* (%) unless otherwise indicated. DQI, Diet Quality Index; MDS, Mediterranean diet score; NBDPS, National Birth Defects Prevention Study.
[2] Smoking anytime from 1 mo before to 3 mo after conception.
[3] Folic acid supplements taken from 1 mo before to 3 mo after conception, with or without a multivitamin.
[4] Values are mean scores ± SDs.

"other" race/ethnicity group. In addition, the DQI findings remained unchanged among Hispanics when we further stratified by birthplace (United States, non–United States), smoking status, preconception BMI, periconceptional folic acid–containing supplements, maternal age, and maternal education. A similar stratification approach was used for assessing the MDS overall and within the Hispanic subgroup. Specific individual MDS components (i.e., fruits, grains, sweets, vegetables, fish, legumes, fat ratio, meat, or dairy) did not explain these findings overall or among Hispanics (data not shown). For the MDS, stratified analysis only revealed differences in birthplace. The risk of gastroschisis was statistically significantly reduced with increasing diet quality among women born outside the United States: quartile 2, aOR = 0.62 (95% CI: 0.33, 1.16); quartile 3, aOR = 0.51 (95% CI: 0.28, 0.94); and quartile 4, aOR = 0.50 (95% CI: 0.28, 0.90), compared with

TABLE 3 aORs with 95% CIs for DQI and MDS quartiles for all gastroschisis cases and stratified by maternal race/ethnicity, NBDPS,1997–2009[1]

	DQI					MDS				
	1	2	3	4	*P*-trend[2]	1	2	3	4	*P*-trend[2]
All										
Controls, *n*	2577	2269	2307	2330		2421	2492	2300	2270	
Cases, *n*	373	264	236	252		384	313	232	196	
aOR[3] (95% CI)	ref	0.88 (0.73, 1.06)	0.79 (0.64, 0.96)	0.81 (0.64, 1.02)	0.03	ref	0.96 (0.81, 1.15)	0.85 (0.70, 1.04)	0.78 (0.62, 0.97)	0.014
NH whites										
Controls, *n*	1806	1491	1335	971		1846	1699	1279	779	
Cases, *n*	225	140	116	98		278	156	96	49	
aOR[4] (95% CI)	ref	0.99 (0.77, 1.27)	0.90 (0.68, 1.18)	1.07 (0.77, 1.48)	0.93	ref	0.82 (0.65, 1.02)	0.86 (0.66, 1.12)	0.85 (0.60, 1.20)	0.17
Hispanics										
Controls, *n*	303	418	548	917		178	345	594	1069	
Cases, *n*	88	70	75	116		43	91	87	128	
aOR[4] (95% CI)	ref	0.58 (0.40, 0.86)	0.53 (0.36, 0.79)	0.49 (0.32, 0.76)	0.002	ref	1.30 (0.84, 2.02)	0.82 (0.53, 1.27)	0.85 (0.56, 1.29)	0.04
Other										
Controls, *n*	467	359	422	440		394	448	426	420	
Cases, *n*	60	54	45	38		63	66	49	19	
aOR[4] (95% CI)	ref	1.09 (0.71, 1.69)	0.93 (0.58, 1.50)	0.78 (0.46, 1.37)	0.34	ref	1.13 (0.76, 1.69)	1.08 (0.70, 1.65)	0.64 (0.36, 1.14)	0.24

[1] aOR, adjusted OR; DQI, Diet Quality Index; MDS, Mediterranean diet score; NBDPS, National Birth Defects Prevention Study; NH, non-Hispanic; ref, reference.
[2] Cochran-Armitage trend test.
[3] Logistic regression models adjusted for energy intake (kcal), maternal age, prepregnancy BMI, smoking, and race/ethnicity.
[4] Logistic regression models adjusted for energy intake (kcal), maternal age, prepregnancy BMI, and smoking.

those born in the United States: quartile 2, aOR = 0.97 (95% CI: 0.81, 1.17); quartile 3, aOR = 0.87 (95% CI: 0.71, 1.07); and quartile 4, aOR = 0.84 (95% CI: 0.65, 1.08). Among foreign-born mothers, the majority of women reported their ethnicity as Hispanic (72% cases; 66% of controls) compared with non-Hispanic white (10% cases; 12% controls) and other race/ethnicity (18% cases; 22% controls). A crude assessment of acculturation among Hispanics in this study, as measured by birthplace, showed similar findings in the highest DQI quartiles (quartiles 3 and 4) among U.S.-born Hispanics [quartile 3, aOR = 0.54 (95% CI: 0.33, 0.88); quartile 4, aOR = 0.52 (95% CI: 0.30, 0.91] compared with non–U.S.-born Hispanics [quartile 3, aOR = 0.56 (95% CI: 0.27, 1.19); quartile 4, aOR = 0.54 (95% CI: 0.25, 1.16)]. Among all Hispanics, the association with MDS was not explained by smoking status, periconceptional folic acid–containing supplements, maternal age, or maternal education.

Discussion

We observed a decrease in the risk of gastroschisis with increasing diet quality, as measured by both the DQI and MDS. However, since most of the 95% CIs included 1, these estimates were not statistically significant. Stratification by maternal race/ethnicity for the DQI revealed a 42–48% reduction in the risk of gastroschisis with increasing diet quality among Hispanic women, whereas for both the non-Hispanic white and "other" race/ethnicity groups no statistically significant associations were observed. Thus, the overall finding of a decrease in risk with increasing DQI scores was driven by Hispanic women, and this association was not explained by maternal age and education, place of birth, prepregnancy BMI, periconceptional smoking, or periconceptional folic acid–containing supplement intake. The finding of a decrease in risk with increasing diet quality measured by the MDS was driven by women born outside the United States, primarily Hispanics, with a 50% reduction in risk between the highest and lowest quartiles.

Our findings of a decreased risk with increasing diet quality among Hispanics and women born outside the United States have not previously been reported for gastroschisis and must be considered in light of the study's limitations. The most recent U.S. data suggest that diet quality, as measured by the Healthy Eating Index–2005, is not optimal and has changed little between 1994–1996 and 2001–2002 (36), without much improvement between 2001–2002 and 2007–2008 (37). Although several studies suggest that Hispanics have better quality diets (7,38), these findings are not consistent among all studies (39) because of challenges in understanding how to appropriately measure acculturation and its impact on diet (40). Hispanic ethnicity was self-reported and represents a culturally heterogeneous group. Recent census data found that the majority (70.9%) of Hispanics living in the United States had origins in Central America, with 88% of these being Mexican (41). Culture-driven dietary preferences vary between Hispanic/Latino groups (37) with acculturation influencing their dietary intake (42); these differences are likely incompletely captured in the shortened version of the semiquantitative FFQ (29) because of the limited number of food items that are evaluated. However, we recognize that our subgroup analyses to assess acculturation among Hispanic women, for both the DQI and MDS, may be a result of chance. Finally, recall bias would likely not explain our findings because there is no obvious reason why food intake would be systematically reported erroneously in cases compared with controls.

Strengths of this study include its size, the population-based structure, and the careful clinical case review leading to a well-characterized case group (28). Study sites used a standard protocol for ascertainment and interviewing, which would reduce the potential for selection and participation bias, known challenges with case-control studies (28). Systematic bias in exposure assessment was minimized by the use of trained interviewers using the structured and scripted CATI, and participation overall did not differ between cases (67.4%) and controls (64.8%). Sample size permitted the exclusion of women reporting extreme values and the stratification by several covariates. Using this approach in previous studies has demonstrated different findings (16,23,25), which suggest that the methodology used to assess diet quality is sound and not all birth defects share the same risk associated with poor nutrition. The semiquantitative FFQ is a validated instrument that provided the necessary information to assess diet quality. Scoring for the DQI was based on the 2000 dietary guidelines and the 1992 food guide pyramid, whereas the MDS is based on the number of servings/d of specific foods, which is based on the healthy Mediterranean diet.

Proper nutrition is known to reduce many adverse pregnancy outcomes, including birth defects (8,43). Thus far, evidence with regards to poor nutrition as a risk factor for gastroschisis has been sparse and inconsistent (18–21). More recently, Paranjothy et al. (26) reported a statistically significant reduction in the risk of gastroschisis with increasing fruit or vegetable intake during the first trimester. Our analysis did not support this finding (both diet quality scores include fruits and vegetables), either when evaluating total scores of the DQI and MDS or when evaluating the decile ranking of fruit and vegetable consumption before summing the total scores for the DQI and MDS.

Eating a healthy diet is an important message to convey to all women of childbearing age because many adverse pregnancy outcomes are related to poor nutrition. In this study, higher diet quality as measured by the DQI and MDS was inversely correlated with the risk of gastroschisis, but only among Hispanic women. Higher diet quality, as measured by the MDS, was associated with a lower risk of gastroschisis among women born outside of the United States. The DQI and MDS findings were not influenced by maternal age in this study. Replicating and expanding these findings in other populations will help confirm or refute whether higher diet quality, race/ethnicity, and maternal birthplace play roles in reducing a woman's risk of gastroschisis.

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